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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,127	11/19/2001	Tony Peled	00/21438	8221

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	19

DATE MAILED: 08/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,127	PELED ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-100* is/are pending in the application.

4a) Of the above claim(s) *44-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 37-100 are pending.

Applicant's election of Group I, claims 37-43 and tetraethylenepentamine (TEPA) as specific transition metal chelator, in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 44-100 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 37-43 , as they all read on a method of in vivo expanding a population of cell, while at the same time inhibiting differentiation of said cells wherein , tetraethylenepentamine (TEPA) is specific transition metal chelator, are under consideration in the instant application.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Israel on 08/17/1999. It is noted, however, that applicant has not filed a certified copy of the IL 99/00444 application as required by 35 U.S.C. 119(b).

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of *ex-vivo* expanding a population of CD34+ cells while at the same time inhibiting differentiation of said cells, the method comprising a step of providing CD4+ *ex-vivo* with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper, does not reasonably provide **enablement** for a method of *in-vivo* expanding a population of any cells while at the same time inhibiting differentiation of said cells, the method comprising a step of providing any cells with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses that providing $CD4^+$ cells *ex-vivo* with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper, only $CD4^+$ cells expanding and at the same time inhibiting differentiation (see examples 1 and 2 in particular).

The specification does not adequately teach how to effectively expand and at the same time inhibit differentiation of *any* cells *in vivo* by providing said cells with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper.
The specification does not teach how to extrapolate data obtained from $CD4^+$ cells *ex-vivo* assay studies to the development of effective *in vivo* protocols for imposing proliferation and at the same time restricting differentiation of *any* cells by providing said cells with conditions that reduces the capacity of said cells in utilizing copper. In addition, no animals were used as model system to effectively expand *any* cells *in vivo* by providing said cells with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper . Since there is no animal model system in the specification to effectively expand *any* cells *in vivo* it is unpredictable how to correlate *in vitro* results with *in vivo* use. Thus in the absence of working *in vivo* examples or detailed guidance in the specification, the intended uses of a method of *in-vivo* expanding a population of any cells while at the same time inhibiting differentiation of said cells, the method comprising a step of providing any cells with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper are fraught with uncertainties. Moreover, Applicant himself acknowledge that the mechanism of the effects of cupper is unknown (see page 3, line 35-37 in particular). As such, the invention must be considered unpredictable. In addition, Percival (Am .J. Clin. Nutr. 1998, Vol.67 p.1064-1068) teaches that the role of copper in effecting cellular function is contradictory and that more studies have to be done to understand the mechanisms by which copper effect the process of differentiation in various types of cells (see entire document, pages 1064 and 1066 in particular).

Also an issue that claimed method of *in-vivo* expanding a population of any cells while at the same time inhibiting differentiation of said cells, comprising a step of providing conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper. This step comprises administering *in vivo* a transition metal chelator which binds copper such as ethylendiamine or tetraethylenepentamine (TEPA). However, according to ChemMaster Safety Data Sheet (1999, pages 1-4) and The Merk Index (1983, Tenth edition, page 3742) ethylendiamine or tetraethylenepentamine (TEPA) are helth hazards and care must be taken in handling because of the caustic nature of ethylendiamine or tetraethylenepentamine (TEPA) and since it may cause allegic respiratory reaction, headaches, nausea and dizzness. Thus in the absence of working *in vivo* examples the in vivo use of a transition metal chelator which binds copper such as ethylendiamine or tetraethylenepentamine (TEPA) is considered potential health hazard.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of *in-vivo* expanding a population of any cells while at the same time inhibiting differentiation of said cells, the method comprising a step of providing any cells with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. No claim is allowed.

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
August 5, 2003.

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600